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IN BRIEF

METABOLIC DISEASE

PGC1α inhibition ameliorates diabetes

Peroxisome proliferator-activated receptor-γ co-activator 1α (PGC1α) plays a pivotal part in energy homeostasis and is involved in the regulation of gluconeogenesis. Using a cell-based high-throughput chemical screen, Sharabi *et al.* have identified a small molecule, SR-18292, that increases acetylation of PGC1α, which results in suppression of gluconeogenic gene expression and reduced glucose production in primary hepatocytes. In dietary and genetic mouse models of type 2 diabetes, injection of SR-18292 reduced glucose production, increased insulin sensitivity and improved glucose homeostasis, without signs of toxicity.

ORIGINAL ARTICLE Sharabi, K. *et al.* Selective chemical inhibition of PGC-1α gluconeogenic activity ameliorates type 2 diabetes. *Cell* **169**, 148–160 (2017)

AGEING

FOXO4 inhibition eliminates senescent cells

Senescent cells exhibit a pro-inflammatory phenotype, and are thought to accelerate ageing and the onset of age-related diseases. Baar *et al.* report a key role for forkhead box protein O4 (FOXO4) in maintaining senescent cell viability. *In vitro*, a FOXO4-derived peptide designed to inhibit the interaction of this transcription factor with the tumour suppressor p53 reduced senescent cell viability through p53-mediated cell-intrinsic apoptosis. In mice, the FOXO4-derived peptide counteracted doxorubicin-induced chemotoxicity and restored fitness, fur density and renal function in models of ageing.

ORIGINAL ARTICLE Baar, M. P. *et al.* Targeted apoptosis of senescent cells restores tissue homeostasis in response to chemotoxicity and aging. *Cell* 169, 132–147 (2017)

CYSTIC FIBROSIS

Thymosin α1 rescues CFTR activity

Cystic fibrosis is caused by mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein and is characterized by chronic lung inflammation. Romani *et al.* show that the naturally occurring polypeptide thymosin α1 — clinically used as an immunotherapeutic agent — not only limited the inflammatory response when injected into a mouse model of cystic fibrosis, but also rescued the activity of CFTR in these mice and in human bronchial epithelial cells from subjects carrying *CFTR*^{F508del} (the most common mutation among individuals with cystic fibrosis).

ORIGINAL ARTICLE Romani, L. *et al.* Thymosin α1 represents a potential potent single-molecule-based therapy for cystic fibrosis. *Nat. Med.* http://dx.doi.org/10.1038/nm.4305 (2017)

INFLAMMATION

Oncostatin M blockade attenuates colitis

Anti-tumour necrosis factor (TNF) antibodies represent established therapies for inflammatory bowel disease (IBD), but up to 40% of patients exhibit primary nonresponsiveness to anti-TNF agents, and resistance can develop. West *et al.* observe high levels of the cytokine oncostatin M (OSM) and its receptor (OSMR) in inflamed intestinal mucosa from patients with IBD, which is associated with decreased responsiveness to anti-TNF therapy. In a mouse model of anti-TNF-resistant intestinal inflammation, genetic deletion of OSM or treatment with an Fc-tagged soluble OSMR–interleukin-6 receptor subunit-β fusion protein significantly suppressed colitis.

ORIGINAL ARTICLE West, N. R. *et al.* Oncostatin M drives intestinal inflammation and predicts response to tumor necrosis factor–neutralizing therapy in patients with inflammatory bowel disease. *Nat. Med.* http://dx.doi.org/10.1038/nm.4307 (2017)

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